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February 8, 2002

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on General Electric's HPV Test Plan for Phosphite Isodecyl/Phenyl Chemical Category

Dear Administrator Whitman:

The following comments on General Electric's (GE's) test plan for the phosphite isodecyl/phenyl chemical category are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than nine million Americans.

GE's test plan for the phosphite isodecyl/phenyl chemical category reflects a distinct improvement over previous submissions. GE has worked to develop a more thoughtful approach to the analysis of these chemicals and has developed a defensible category of four organophosphite chemicals with similar physicochemical and toxicological properties. GE has presented a systematic analysis of the structural patterns of the chemicals and has correlated these with trends in toxicity.

However, GE has inappropriately proposed unnecessary tests on animals. GE has proposed two acute aquatic toxicity tests on fish and two combined repeat dose/reproductive/developmental toxicity tests. These tests will kill as many as 920 animals.

The test plan specifically violates the following terms of the October 1999 Agreement among the EPA, industry, and health, animal protection, and environmental organizations, which delineated certain animal protection measures:

2. Participants shall maximize the use of existing and scientifically adequate data to minimize further testing.

3. Participants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships

Additional acute fish toxicity tests are unnecessary because they have already been conducted on two of the

four category members. Both these test results indicated that the LC50 was greater than the maximum soluble concentration. More fish tests will not enhance the understanding of these chemicals, which appear to exhibit very low toxicity to the fish already subjected to limit doses of these chemicals.

Furthermore, GE has not yet gathered information on the stability, solubility, and partitioning of these chemicals in water. Since these chemicals are not likely to be soluble in water, the physical, chemical, and environmental fate data may also provide further evidence that additional fish toxicity tests are unnecessary. This information will most likely confirm that these chemicals are not likely to produce a hazard in an aquatic environment.

Finally, given the availability of nonanimal methods, any further testing on fish is inappropriate. This is an ideal situation for applying ECOSAR, since experimental data are available for two category members, allowing for a trend analysis.[1] ECOSAR is an established QSAR program that estimates toxicity to fish, invertebrates, and algae.

In vitro tests with the protozoan *Tetrahymena* are frequently used as a measure of aquatic toxicity in ecological risk assessments.[2] The biochemistry and physiology of *Tetrahymena* have been thoroughly investigated since the 1950s, and *Tetrahymena*, especially *T. pyriformis*, have been used for aquatic toxicity testing since the 1970s. Moreover, the genomics of the organism are currently being elucidated. The *T. pyriformis* population growth test is quick, easy, and cheap, and has great breadth.[3]

The EPA has a massive database on the acute toxicity of more than 600 organic chemicals to fish called "Acute Toxicities of Organic Pollutants to Fathead Minnows (*Pimephales promelas*)." Comparisons of toxicity test results from the *in vitro* TETRATOX assay and the EPA's fish acute toxicity data have yielded good correlation between the two methods.[4] Evaluation of *in vitro* and *in vivo* aquatic toxicity data have allowed researchers like Schultz and colleagues to develop models to predict toxicity based on quantitative structure activity relationships, QSARs.[5-7] Both the *in vitro* TETRATOX assay as well as QSARs provide more humane, efficient methods to predict aquatic toxicity at the screening level. We have an ongoing dialogue with the EPA about the incorporation of these alternative, nonanimal methods into the HPV program.

While the systematic evaluation of the compounds' toxicology laid out in this test plan is commendable, the analysis presented here could be expanded further. In its previous submissions, GE proposed extensive animal testing on three individual chemicals, including tris(nonylphenyl)phosphite and phosphorous acid, cyclic neopentanetetrayl diphenyl ester. The previous GE test plans represented gross violations of the terms and spirit of the October 1999 Agreement. After discussions with our organizations, GE agreed to defer most mammalian testing until November 2001. (They refused to defer the reproductive toxicity tests and initiated acute toxicity tests in November 2001, without waiting for EPA's forthcoming guidance on the incorporation of the *in vitro* cytotoxicity tests. In the spirit of transparency, GE should resubmit its revised test plans for these chemicals and provide any results.) GE did not consider incorporating the individual organophosphite compounds into a broader category, which could have reduced the numbers of animals killed in these toxicity tests.

GE can expand its analysis beyond isodecyl substitute phenyl phosphates presented in this plan and consider other substitutions on the phenyl group in its analysis. For example, considering data from the nonylphenol analysis would be a first step in expanding this analysis. A brief list of other phenyl-phosphorus antioxidant stabilizers that are good candidates for inclusion into this group is presented in Table 1 of our comments on the tris(nonylphenyl)phosphite plan, which can be viewed at *http://www.epa.gov/chemrtk/phsphite/trispcrmct.pdf*. The expansion of this category could eliminate the perceived need for additional repeat dose/

reproductive/developmental tests.

We commend GE for the formation of a strong chemical category in this current test plan for phosphite isodecyl/phenyl compounds. This test plan is certainly a step in the right direction. However, we urge GE to consider including the results from its tests with similar chemicals in this analysis.

Organophosphorous compounds are recognized as toxic chemicals, with the main endpoint of concern being neurotoxicity. Organophosphorous esters are associated with delayed neurological effects as well as dermal and eye irritation. Triphenyl phosphite exhibits symptoms similar to those caused by phenols: dizziness, muscle weakness, dimness of vision, ringing in the ears, irregular and rapid breathing, weak pulse, and shortness of breath. All these may be followed by loss of consciousness, collapse, and death.

GE and the other members of the Phosphite Producers HPV Consortium should focus on reducing human exposure to these chemicals to the lowest level feasible rather than subjecting more animals to unreliable tests.

Thank you for the opportunity to comment. I can be reached at 202-686-2210, ext. 302, or via e-mail at *ncardello@pcrm.org.* Correspondence should be sent to my attention at PCRM, 5100 Wisconsin Ave., N.W., Suite 400, Washington, DC 20016. I look forward to your response on these important issues.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist

References

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